



Recent research trends in Kawasaki disease-related infection

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Key message

The incidence of Kawasaki disease has reportedly decreased since the coronavirus disease 2019 (COVID-19) quarantine. However, multisystem inflammatory syndrome in children has reportedly occurred more frequently in areas where COVID-19 was prevalent than in previous years. Research into the etiology of childhood and adolescent systemic vasculitis in infection-related immune responses during the COVID-19 pandemic has increased accordingly.

Kawasaki disease (KD), first described in 1967 by Japanese pediatrician Tomisaku Kawasaki, is a vasculitis of undetermined etiology that usually affects the medium-sized vessels of children under 5 years of age. The leading theory for its pathogenesis is that an unknown infectious agent activates the immune system of a genetically susceptible child.

A nationwide survey using KD patient data has been conducted in South Korea every three years since 1994.¹⁾ A recent study reported new findings that KD occurs most commonly in the cold winter season (December–January), as shown in most epidemiological studies from countries with four discrete seasons. Compared with previous surveys, the second seasonal peak of KD occurrence in South Korea moved from summer (June, July, and August) to late spring (May and June).¹⁾ Such changes in its seasonal distribution provide potential clues about the causes of KD related to climate change and seasonal epidemics.

Various types of bacteria and viruses are reportedly infectious pathogens related to KD, and several analyses are ongoing. In addition, the geographic patterns of KD occurrence, wherein the incidence of KD in Northeast Asian countries including Japan, South Korea, China, and Taiwan, are 10–30 times higher than those in the United States and Europe.²⁾ Differences in the seasonal incidence of KD outbreaks reported in previous epidemiological studies suggest that seasonal infections may induce specific immunological responses in genetically vulnerable patients. Previous studies also demonstrated that KD is an essential mechanism by which abnormal immune responses after infection occur in individuals with specific genetic backgrounds.

There are various clinical, epidemiological, and pathophysiological aspects of KD-related research; however, the relationship between KD and pathological infection is among the most notable.³⁾ Another aspect that supports its association with infection is the significant characteristic overlap of clinical symptoms of KD and other infectious substances, particularly scarlet fever, newly described multisystem inflammatory syndrome (MIS), and adenovirus.⁴⁾

Since 2019, coronavirus disease 2019 (COVID-19) has spread worldwide and become a global pandemic. In 2020, a KD-like illness, severe MIS in children (MIS-C), was reported in children infected with COVID-19 for the first time in Europe that alarmed pediatricians and has since been reported in several countries worldwide. MIS-C affects children under 19 years of age with active or recent infections of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).^{5–7)} So far, SARS-CoV-2 causes a poorly understood pediatric systemic vasculitis.

After the COVID-19 pandemic reached the Bergamo province of Italy, a 30-fold increase in the incidence of KD-like illness compared to the previous five years was described. In addition, recent reports indicated that the number of KD-like illness cases significantly increased compared to previous years in the United States, Italy, and the United Kingdom, where COVID-19 was more prevalent, increasing expectations that confirm the association between KD and infections.⁸⁾

Recent reports demonstrated that the incidence of KD significantly decreased during the COVID-19 pandemic with the implementation of mask wearing and social distancing measures. The decrease in the incidence of KD is estimated to have been affected by the prevention of the spread of general viral infections through strengthening quarantine measures, which supports the concept that infection is related to KD.^{9,10)}

MIS-C overlaps with myocarditis, toxic shock syndrome, and KD. In particular, it may show signs and symptoms similar to those of KD, but there are several differences. MIS-C is more common in older children than in children with KD, and the most frequent clinical characteristic is gastrointestinal or neurological symptoms. MIS-C often presents with shock, making it difficult to consider the same disease. Therefore, its

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epidemiological, clinical, and immunological differences from KD are distinct.

Based on the COVID-19 pandemic situation, current research trends in KD should further study and analyze similarities and differences in the pathogenesis of KD and MIS-C and focus on etiological studies of childhood and adolescent systemic vasculitis after infection-related immune responses.

See the article “Research trends on the causes of Kawasaki disease focusing on the association with viral infection” via <https://doi.org/10.3345/cep.2022.00150>.

Footnotes

Conflict of interest: No potential conflict of interest relevant to this article was reported.

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